

Because this proposed national advisory body would have a substantial group of public and community representatives, as well as scientific and physician leaders, the advisory committee itself could provide one form of community review and input with regard to the conduct of the study. This input, although remote from the specific community in which the research is to be conducted, would nonetheless provide a unique form of community information and response not available with only local information.

Finally, this national advisory body could provide advice on the methods used by the investigators to inform the local community and to provide the means for receiving community input. The body could also provide reasonable advice on how the local IRB and investigators should respond to objections or concerns expressed by the community or individuals within the community. The specific details of information provided to the community, a detailed listing of expressions of concern or support by the community and the reasonableness of the response would be disclosed to the advisory committee. A very difficult problem would be the serious objection to the conduct of the study by a very small group of individuals within a broader, well-informed community wishing to participate. A national advisory body could provide standards and reasonableness with regard to denying the objections made by a small number of individuals within a large community. A mandatory national advisory group review was not recommended, because it was viewed that this additional step would become another major delay in the conduct of straightforward research under a waiver.

CONCLUSIONS

1. The treatment of cardiac arrest is in desperate need of clinical research on how to improve survival and decrease disability outcomes.
2. The results of enormous efforts to salvage patients from cardiac arrest have been extremely disappointing. These patients are not likely to improve, unless there are fundamental and applied research efforts to produce major advances.
3. A critically important target for resuscitation research is avoidance of severe neurologic disability.
4. Patients in cardiac arrest are unable to provide informed consent. Their disease has deprived them of autonomy. Thus, a strong and thoughtful IRB is critical in assessing the need for and, ultimately, where appropriate, in granting a waiver of informed consent. Advance directives should always be honored.
5. As used in the FDA's regulations on waiver of informed consent, "prospect of direct benefit to the subject" should be taken to mean: 1) the therapy is directed to the patient's condition that required the waiver; 2) there is at least as good a chance of a beneficial result as a deleterious outcome from the intervention; 3) in randomized trials, there is clinical equipoise; and 4) in

nonrandomized trials, the risks and benefits profile of the experimental treatment is at least as favorable as the current standard of care.

6. There is a need for a major educational effort to inform the public and the mass media of these issues, focusing on the importance of waivers of informed consent.
7. The IRBs and investigators should be provided with additional education and support toward implementation of the regulations on waiver of informed consent. The ACC, American Heart Association (AHA), Society for Academic Emergency Medicine (SAEM), American College of Emergency Physicians (ACEP), American Academy of Neurology (AAN), American Society of Anesthesiology (ASA), National Association of Emergency Medical Services Physicians (NAEMSP) and other professional societies should have a leadership role.

The final rule advanced by the FDA in 1996 provides researchers with an opportunity to do resuscitation studies in circumstances in which individual patients are unable to provide prospective informed consent. The final rule clearly states the criteria for applying the waiver of informed consent, but gives limited guidance for its implementation. The number of resuscitation studies for which waiver of informed consent apply is limited, and IRBs and principal investigators may not be familiar or have experience with the regulations providing for waiver of informed consent. A substantial number of questions concerning its implementation have arisen. In addition, to date, there has been limited experience with the new regulations, and no prototype for its implementation exists. Although the FDA promises a guidance statement giving suggestions for implementing the regulations, this statement is still in the process of final approval. Even after it is approved, it is likely that IRBs and investigators will need education and support to implement the regulations. Therefore, we believe that professional organizations such as the ACC, AHA, SAEM, ACEP, AAN, ASA and NAEMSP should develop strategies to educate and support researchers and IRBs in implementing the regulations regarding waiver of informed consent. One strategy might be for each organization to identify experts within its own membership who are familiar with the regulations, understand their purpose and spirit and have some knowledge of existing methods of implementing them. In addition, these organizations should advertise the availability of consultants within the organization who can assist investigators in determining the best methods of implementing the regulations on a protocol-by-protocol basis. These organizations should also make the availability of this expertise known beyond their membership, so that investigators with no official means of receiving such counsel might have the ability to discuss projects and implementation strategies with knowledgeable individuals representing the resuscitation research community as a whole. Organizations should develop didactic pro-

grams regarding implementing the waiver for presentation at national meetings and have literature available for researchers. The support and education regarding implementation of the regulations given by these various professional organizations may require some financial assistance of the organizations. This commitment is an important mission of these professional organizations, whose members include resuscitation researchers committed to advancing the emergency care of their patients and society.

The ACC should, as a consequence of this 31st Bethesda Conference, be positioned to rapidly provide input to the anticipated FDA-drafted guidance document on implementation of the regulation on waiver of informed consent.

The 1996 FDA regulations provide for waiver of informed consent in life-threatening emergencies. Unfortunately, there is a widespread misunderstanding among sponsors, clinical investigators and IRBs of some of the provisions of the regulations, particularly with respect to the degree to which participation in the study must provide a positive benefit to each individual subject and in the areas of community consultation and public notification. A draft guidance document that addresses all aspects of the informed consent waiver process is in final preparation at FDA. The ACC should actively participate in public comment on the draft guidelines.

8. An official advisory group should serve as an optional resource to local IRBs, the FDA, sponsors and individual or groups of investigators, and may be called on for advice by any of these sources. This group should be constituted under the auspices of a concerned federal government body.

Many IRBs are reported to be unfamiliar with or uncertain as to how to practically apply the waiver of informed consent regulation. In addition, FDA staff, sponsors or groups of investigators may have internal disagreements on how to discharge their responsibilities with regard to a proposed investigation. The conferees believe that for these groups, and where a protocol will involve multiple centers and hence multiple IRBs, it would be valuable to have an authoritative independent national forum. This optional forum would provide broadly applicable evaluation and advice on how to meet the requirements of the waiver regulation before consideration of a given protocol on an institution-by-institution basis. Therefore, the conferees recommend that the federal government make available an advisory committee to provide review, on a request basis, of clinical investigations that plan to use the waiver of informed consent provisions. This committee, modeled after RAC, might be either an independent advisory committee for these specific issues or a panel constituted under the charter of an existing committee with appropriate jurisdiction (e.g., an FDA advisory committee supplemented with patient or public representatives and

specialists in bioethics and communication). The advisory committee should, in conjunction with its secretariat, have the discretion to accept for review and discussion those topics which give rise to significant new issues and decline any issues believed to be settled by previous similar experience or better handled at the local IRB level. The scope of the advice offered should include the full range of likely controversial topics raised by the waiver regulations or available guidance on implementation of them. This would include the ethics of informed consent waiver in a given protocol, the scientific support for the proposed study, whether there is clinical equipoise regarding the treatments, trial design issues, the appropriateness and adequacy of the proposed mechanism for public input and informing the public of the trial.

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